UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA LISBOA

TRABALHO FINAL
MESTRADO INTEGRADO EM MEDICINA

Instituto de Medicina Preventiva e Saúde Pública

INSTRUMENTOS DE RASTREIO E DIAGNÓSTICO DE DELIRIUM EM DOENTES IDOSOS

Mafalda Sofia Batista Sequeira

MAIO'17

LISBOA
UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA LISBOA

TRABALHO FINAL
MESTRADO INTEGRADO EM MEDICINA

Instituto de Medicina Preventiva e Saúde Pública

INSTRUMENTOS DE RASTREIO E DIAGNÓSTICO DE DELIRIUM EM DOENTES IDOSOS

Mafalda Sofia Batista Sequeira

Orientado por:

Dra. Ana Sofia Baptista Duque

MAIO'17

RESUMO

O envelhecimento da população constitui uma das maiores preocupações da sociedade moderna do século XXI. Nas últimas décadas assistimos a um aumento da esperança média de vida concomitantemente com o declínio da natalidade o que contribuiu para o envelhecimento da população nos países desenvolvidos. Portugal não é exceção no que toca à idade média da sua população, sendo que no nosso país a esperança média de vida, à nascença, é de 78 anos para os homens e 84,4 para as mulheres indo estes valores de encontro aos dos restantes países da União Europeia. (PORDATA 2014). (16)
Os portugueses estão em quarto lugar, atrás apenas de França (88,6), Espanha (88,1) e Suíça (87,7), um pódio a cinco completado pela Eslovénia (87,4), estimando-se que em 2030 apresentem esperança média de vida de 87,4 anos. (2) De acordo com as últimas avaliações, os portugueses já estão a viver uma média de 81,1 anos.
Como é do conhecimento geral não é prevista inversão neste indicador, sendo que, segundo as mais recentes projeções demográficas prevê-se que em 2050 três em cada dez pessoas terá 65 anos ou mais.

Este aumento da esperança média de vida é influenciado por vários fatores macrossociais como seja a capacidade de distribuição de rendimentos, os sistemas de saúde e segurança social e a educação. Estes fatores definem a capacidade de um país gerar riqueza e, consequentemente, de garantir qualidade de vida à sua população. Esta irá refletir-se em termos individuais em anos de vida, já que estes fatores macrossociais acabam por resultar num melhor acesso aos cuidados de saúde e num comportamento ativo face a saúde e a doença. Fazendo um enfoque no acesso aos cuidados de saúde, como um dos principais fatores para o aumento da esperança média de vida de uma sociedade, foi de extrema importância a rede de cuidados de saúde primária de carácter preventivo para o envelhecimento ativo e com qualidade de vida.

O envelhecimento é um fator positivo quer individualmente quer globalmente para as sociedades, sendo o reflexo do progresso económico, social e dos sistemas de saúde das mesmas. Individualmente, o aumento da longevidade trouxe alterações evidentes no que concerne à participação dos idosos na vida social e ao seu estado de saúde. Viver mais

implica também estar mais exposto a doenças crónicas, bem como, ao declínio das redes sociais e pessoais. A longevidade é, muitas vezes, sinónimo de perda de autonomia e independência, o que muitas vezes se torna um problema não só para o idoso como para o cuidador e para a sociedade. O avançar da idade traduz-se no aumento da vulnerabilidade do estado de saúde, no isolamento social e no aumento de um dos fatores que mais contribui para a dependência física, mental e económica que é a solidão. Contudo, estas não são condições inevitáveis do envelhecimento, sendo possível haver um envelhecimento saudável, ativo, bem-sucedido, com qualidade de vida para o individuo e beneficio para a sociedade.
O envelhecimento representa também um impacto significativo no sistema de saúde de um país, quer estejamos a falar de cuidados primários ou hospitalares.

Na minha experiência como aluna do último ano do curso de Medicina, durante os meus estágios nas enfermarias de Medicina Interna dos diferentes hospitais da região de Lisboa, constatei que a idade média dos doentes internados ultrapassava os 75 anos. No decorrer dos meus últimos dois anos como estudante de Medicina, que são os anos que envolvem mais prática clinica, constatei que a larga maioria da população hospitalizada nas enfermarias eram idosos com pluripatologia e plurimedicados. Outro aspeto que despertou a minha atenção e mesmo o meu interesse pela área da Geriatria foi o facto de que, de uma forma geral, a maioria dos profissionais de saúde não está preparada/treinada para lidar com uma população envelhecida com múltiplas co morbilidades e síndromes geriátricos. Com isto quero dizer que, é evidente a falta de investimento na formação dos profissionais de saúde no geral, na área da Geriatria face a condição demográfica do nosso país.

A razão pela qual escolhi realizar o meu trabalho final de mestrado na área da geriatria prende-se, por um lado, com o facto de a minha maior área de interesse dentro das especialidades médicas ser a Medicina Interna. A Medicina Interna em ambiente hospitalar, bem como, a Medicina Geral e Familiar no contexto dos cuidados primários são áreas em que uma grande percentagem dos doentes são doentes geriátricos. Os estágios em medicina interna fizeram-me perceber que, para lidar com a realidade demográfica do nosso país que é importante investir em formação na área da Geriatria, bem como desenvolver abordagens especificas e especializadas para lidar com estes pacientes. A Geriatria demonstrou ser uma subespecialidade aliciante, na medida em que,

envolve um grande investimento no doente, uma grande preocupação com o seu estado físico, psicológico e social e um grande envolvimento com os fatores que globalmente podem contribuir para a sua fragilidade quer sejam eles os fatores relacionados com a sua patologia orgânica, com a plurimedicação ou mesmo relacionados com o cuidador. Este investimento numa avaliação e intervenção holística, centrada na pessoa, têm potencial impacto na sua qualidade de vida.

O meu trabalho foca um quadro orgânico particular, o Delirium, quadro esse que não é exclusivo da população geriátrica sendo, no entanto, mais prevalente nesta população. O Delirium é uma síndrome cerebral orgânica potencialmente reversível de início agudo, caracterizada por desatenção, perturbação na cognição e / ou alteração na perceção. Esta condição é muito comum em pacientes hospitalizados vulneráveis , tal como os idosos com pluripatologia. Estima-se que o Delirium afete 14-56% de todos os idosos hospitalizados. Durante os meus estágios nas enfermarias de Medicina Interna assisti, não poucas vezes, a quadros consistentes com Delirium serem rotulados como Défices cognitivos ou Demências sem que antes fossem aplicados instrumentos de avaliação específicos para aferir um diagnóstico definitivo.

O motivo pelo qual escolhi desenvolver o tema sob a forma de um artigo de revisão, prende-se com a oportunidade de treinar a elaboração de um documento integrador de conceitos e estado de arte possível de publicar, com potencial para disseminar o conhecimento. Sendo, como já referi anteriormente, a minha área de interesse a Medicina Interna e em particular a Geriatria perspetiva-se que, futuramente, este tipo de comunicação volte a ser repetido durante a minha carreira médica e formação pós-graduada. A opção pela escolha da língua inglesa prende-se com o facto de as publicações nesta língua aumentarem a comunidade científica capaz de ler e discutir o artigo, o que é crucial para evolução da ciência.
Em resumo, a minha escolha em relação a este tópico, é devido não apenas ao meu interesse em Geriatria, mas também ao fato de ter assistido à “rotulagem” de pacientes idosos com demência, várias vezes, quando o diagnóstico correto era Delirium com repercussão negativa no seu tratamento e prognóstico. E por que é que isso acontece? Talvez devido à falta de formação dos profissionais de saúde em geral, a falta de informações sobre o status inicial do paciente ou à fraca difusão das escalas diagnósticas de Delirium entre médicos e enfermeiros.

A minha tese enfoca as escalas diagnósticas mais utilizadas e difundidas de Delirium em sistemas de saúde nacionais e internacionais, referindo-se às suas principais características, bem como seus prós e contras.

Idealmente, gostaria que meu trabalho contribuísse para um uso mais regular das escalas de diagnóstico de Delirium nas enfermarias de nosso país, no sentido de um diagnóstico mais precoce e assertivo.

Palavras Chave: Envelhecimento, Geriatria, Delirium, Ferramentas de diagnóstico e rastreio.

ABSTRACT

Delirium is a common and serious problem among acutely ill persons. It is estimated that delirium affects 14-56% of all hospitalized elderly patients. This syndrome is characterized by inattention, disturbance in cognition and/or alteration in perception and is linked to higher rates of mortality, institutionalisation functional and cognitive decline, it remains underdiagnosed. Careful consideration of its phenomenology is warranted to improve detection and therefore mitigate some of its clinical impact.

The current standard for the diagnosis of delirium is based on DSM-5 (Diagnostic Manual of Mental Diseases version 5) but over the years many scales have been designed for screening, diagnosis and assessing the severity of delirium. This paper intends to review the various instruments available to screen the patients for delirium, instruments available to diagnose delirium, assess its the severity, cognitive functions, motoric subtypes, aetiology and associated distress.

Among the various screening instruments, the Confusion Assessment Method CAM is considered to be the most useful instrument because of its accuracy, brevity, and ease of use by clinicians and lay interviewers. When comparing the tools, the CAM although it is the most widely used, studied and disseminated and it takes few time to be completed, it seems more difficult to complete by non-psychiatry experts, who may have some difficult to match the patients changes to the features identified in the CAM criteria. For research purposes, it is probably the better option even because it has been used for 16 years, enabling comparisons between centres.

Regarding the new scales, the advantaged of 4AT(Assessment test for Delirium and Cognitive impairment) is that the instructions given to the healthcare professional to assess each delirium dimension are very clear and easy to understand and perform, which makes 4AT a nurse-friendly tool. Also its layout is very simple. 4AT is therefore a convenient tool to be used in clinical settings where gerontopsychiatry and geriatrics education and skills are low.

Key words: Aging, Geriatrics, Delirium, Diagnosis and screening tools.

O trabalho final exprime a opinião do autor e não da FML.

INDÍCE

Resumo…….. Páginas 3-6

Abstract……..Páginas 7-8

Instrumentos de rastreio e diagnóstico de Delirium em doentes idosos

Introdução……. Páginas 10-13
Critérios do DSM V……..Página 14
Comparação entre DSM IV e DSM V……Página 15
Ferramentas de Diagnóstico de Delirium…….Páginas 16-27
Novas tecnologias aplicadas ao diagnóstico de Delirium……Páginas 28-29

Conclusão ……. Páginas 30-31

Tabelas……..... Páginas 32-36

Bibliografia…….....Páginas 37-38

INSTRUMENTOS DE RASTREIO E DIAGNÓSTICO DE DELIRIUM EM DOENTES IDOSOS

SCREENING AND DIAGNOSIS TOOLS OF DELIRIUM IN OLDER PATIENTS

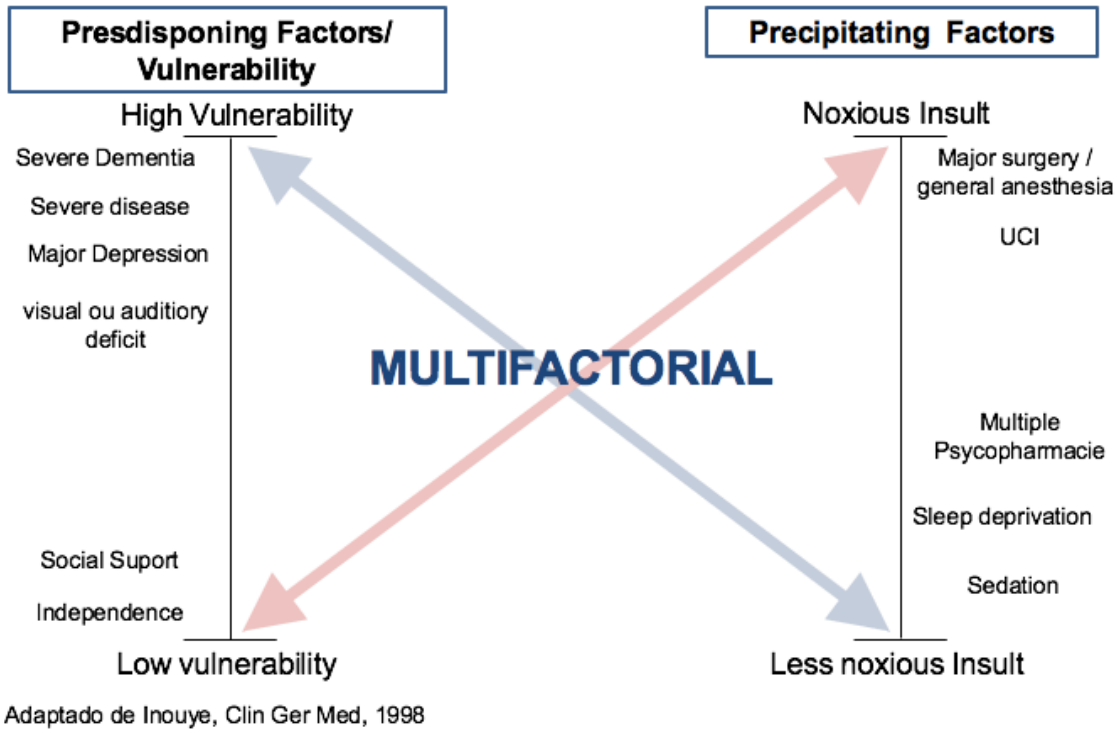
INTRODUCTION

Delirium is an acute onset potentially reversible organic brain syndrome, characterized by inattention, disturbance in cognition and/or alteration in perception. It is considered as an altered mental state, which is somewhere on the continuum between coma and stupor in one side and normal wakefulness and alertness in the other side. Main features are fluctuation of mental state and underlying medical disorders, making this condition very common in hospitalized vulnerable older patients. It is estimated that delirium affects 14-56% of all hospitalized elderly patients.(3) Few studies have been conducted in medical wards in Portugal showing prevalence of delirium between 15% and 80%.(18) This significant difference in prevalence of delirium might be explained by the poor awareness of the importance and features of this condition, lack of validated screening and assessment tools for Portuguese population and lack of training in applying them. (19) Poor awareness of delirium by health-care professionals in Portugal is, at least, due to under representation in under and post graduated curriculum. Moreover, in clinical practise delirium has been identified using other designations such us: acute confusional state, acute organic brain syndrome or acute organic mental disorder. Use of different designations can preclude standardization of diagnostic criteria, research on delirium and the implementation of prevention and treatment interventions, which will increase delirium occurrence and severity.

Despite several validated tools to screen for delirium in the hospital setting, delirium is misdiagnosed or unrecognized in over half of cases. According Maldonado it is "extremely poorly recognized by physicians, and available tools are just not that great in the real world.

Delirium not only is very frequent in older medical patients, but also it is a severe condition. It is a leading cause of morbidity, increased hospital stay and institutionalization and decreased quality of life. Several other medical complications, including many geriatric syndromes, occur as a complication of delirium such us Pneumonia, urinary infection, pressure ulcers, falls and dehydration.(4)

Indeed, at least 20% of the 12,5 million patients over 65 years of age hospitalized each year in the US experience complications during hospitalization because of delirium. (3)
The physiopathology of this condition is not fully understood and might arise through a variety of different pathogenic mechanisms. Recent research shows that drug toxicity, inflammation and acute stress responses can all contribute to disruption of neurotransmission and ultimately, to the development of delirium.
In older people, gradual accumulation of permanent damage of neurons , dendrites, receptors, and microglia, as well as the impact of cerebrovascular disease or head trauma, may render them, particularly those with underlying cognitive impairment, more susceptible to delirium when biologically stressed.(5) The physiopathology al mechanism and the evidence of it are described in **table 1** page 29.
In spite of the uncertainly about the physiopathology of delirium it is widely known that there are many factors that predisposes and precipitate Delirium.
The occurrence of delirium involves a complex interaction between predisposing factors that became the patient vulnerable to the occurrence of delirium, and precipitating factors, including common insults such as the use of sedatives, sleep privation and major surgery. (5)



Multifactorial model for delirium. The etiology of delirium involves a complex interrelationship between the patient's underlying vulnerability or predisposing factors (left axis) and precipitating factors or noxious insults (right axis). Patient with low vulnerability would develop delirium only with exposure to many noxious insults, such as general anaesthesia and major surgery, ICU stay, multiple psychoactive medications, and prolonged sleep deprivation. Patients with high vulnerability just need a minor insult to develop delirium (Adapted from *Inouye SK. Delirium in hospitalized older patients. Clin Geriatric Med 475,1998)*

Scheme 1

Some authors define older age, prior cognitive impairment, severe illness, psychoactive drug use and sensory impairment as predisposing factors. The environment, drugs, infections, acute illness, neurological conditions and ICU admission have been described as precipitating factors for delirium in elderly patients. (6, 7) Risk factors for delirium have been classified as modifiable and non-modifiable, as shown in table 2 page 29.

A remarkable aspect is that delirium usually results of overlap of several predisposing and precipitant factors at the same time in a single patient, as it occurs in other geriatric syndromes. Awareness of multifactorial nature of delirium is of utmost importance in diagnosing, preventing and treating delirium.

One of the most prominent risk factors for delirium among the elderly patients is dementia, 2/3 of older patients with delirium also present dementia (Delirium superimposed on Dementia).(8)

Clinical experience and recent research on this theme, have shown that delirium can result in permanent cognitive sequelae or even become chronic. In elderly individuals, delirium can be the starting point to cognitive decline, functional decline, loss of independence, institutionalization, and, ultimately death. (6) Delirium can also be the first clue suggesting the existence of cognitive decline, even though it has not been diagnosed before delirium.

There is no single laboratory or imaging test that enables the diagnose of delirium. The diagnose of delirium is a clinical diagnose that is based on the query of the patient and/or the family or other caregiver and physical examination of the patient, performed by a trained healthcare professional. To diagnose delirium, it is crucial to compare the current mental and functional status with baseline, which requires a careful premorbid cognitive assessment, usually through information provided by the family or caregivers. Recently the importance of baseline status has been increasingly highlighted by several authors, and it is even mentioned in the new diagnostic criteria, namely the DSM-5 criteria. (9)

Indeed, Delirium DSM criteria have been considered the gold standard. In 2015 new DSM edition was published. Comparison between the old and the new diagnostic criteria is very relevant as it might change delirium diagnosis in clinical practice. In the first part of the article differences between DSM4 and DSM5 will be reviewed.

Another pitfall of Delirium diagnosis is that the fluctuating nature of delirium can make delirium imperceptible to doctors, who frequently are next to the patient just during few minutes each day. Nurses can play an important rule identifying delirium features as they spend more time next to the patient. Therefore, delirium screening tools have been initially developed to be used by nurses, who can alert doctors for the possible occurrence of delirium. Nevertheless, doctors no rarely use delirium screening tools to confirm delirium suspicion, namely when they are not experts in older age psychopathology. In the second part of the article the most important screening tools will be reviewed stressing the existing evidence to use them for an early diagnosis and to improve survival in delirium patients.

The article focus on the main characteristics of the tools used to diagnoses delirium and compare them with each other.

DSM Criteria

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is published by the American Psychiatric Association(APA) and offers to health professionals an international and common language and standard criteria for the classification of mental disorders.

The first DMS (DSM-I) was published in the US, in 1952, with the event of the World War II and the large scale involvement of the US psychiatrists in the selection, processing, assessment and treatment of soldiers. This new reality moved the focus away from mental institutions and traditional clinical perspectives.

The classification of mental disorders has changed over the years. Remarkably, the designation of Dementia changed to Major Neurocognitive Disorder and Mild Neurocognitive disorder in the new DMS-5. The purpose of this modification was to attenuate the prejurious dimension of the expression "Dementia" amongst the society and the healthcare professionals. This modification might be controversial as patients should be cared according their problems and in a centred-patient approach, focusing on quality of life, wellbeing and respect for human dignity, despite the medical condition, they present reversibility and prognosis. Indeed, the new DSM-5's designations should have little effect on the diagnosis and treatment of patients. More than a modification of designations for the same diseases it is important the change of mentalities and the investment in adequate training. Dementia patients should not be faced as patients without joy of life and social ties, who do not benefit of treatment of medical conditions and geriatric syndromes, until they reach a terminal stage of advanced dementia.

The current standard for the diagnosis of delirium is based on DSM-5 and criteria are depicted in **table 3 page 30** .(3) New features of delirium diagnosis comparing with the previous DSM-4 are in italic.

Comparison of DSM-III, DSM-IV and DSM-5 criteria for Delirium

The advent of clear diagnostic criteria for delirium in DSM-III in 1980 and subsequent DSM-IIIR in 1989 and the DSM-IV in 1994 has supported considerable growth in research activity in the field of delirium. The DSM-IV criteria provide a highly inclusive description of delirium that has become the preferred diagnostic criteria for both clinicians and researchers. Indeed, this has been considered the gold standard tool to diagnose delirium. However, the fifth revision of DSM-5 provides an opportunity to consolidate the strengths of the DSM-IV delirium description while incorporating findings from most recent research.

The table 2 summarizes the differences between the DSM-III, DSM-IV and DSM-5 delirium diagnostic criteria. DSM III criteria were also included in the table due to its historical meaning as they were used to develop the diagnostic tool Confusion Assessment Method (CAM). Direct comparison between different DSM criteria is not easy as the order that delirium features are presented change according the importance that is given to each feature each time: in DSM-III and IV the main feature is "disturbance of consciousness" while in DSM-5 the focus is in "inattention".

Compared to the previous DSM-IV delirium criteria, in the new DSM-5 criteria no major changes were made in core elements of delirium. However, there are some differences in content and wording of DSM-5 criteria that may impact upon the alignment between DSM-5 and previous criteria and more importantly it could impact substantially both clinical and research delirium diagnosis.

For example, the removal of the term 'consciousness' in DSM-5 criteria and the focus on reduced awareness and inattention might substantially narrow the inclusiveness of the criteria, depending on how strictly this term is interpreted. Indeed, applying new delirium DSM-5 criteria will decrease delirium prevalence, which might be controversial. Nevertheless, this interesting analysis concerning the different wording between DSM-III, DSM-IV and DSM-5 criteria might not be significant to every idiom. For example, in Portuguese language "consciousness" and "awareness" are usually translated to the same Portuguese word ("consciência"); consequently, in Portuguese the replacement of "consciousness" for "awareness" will not change the interpretation of delirium criteria. **Table 4** contains the main differences between DSM-III, DSM-IV and DSM-5 criteria.

DELIRIUM ASSESSMENT TOOLS

In literature, delirium assessment tools have been non consensually classified as diagnostic or screening tools. There are **screening tools**, **diagnostic tools**, both **screening and diagnosis tool**s and **delirium severity assessment tools**. Some tools evaluate specific characteristics of delirium such as attention and cognitive dysfunction. Some tools evaluate the patient with delirium in its global dimension like the IQ Code, others like the delirium rating scale- revised (DRS-R-98) are useful in diagnosis and assessment the severity of delirium. Delirium assessment tools are summarized in **table 5 and 6 in page 33 and 34**.

Diagnostic Instruments

As previously mentioned DSM delirium criteria are the gold standard for delirium diagnosis in older patients, namely when applied by old age psychiatry experts (psychiatrists or geriatricians). Several tools have been developed based on DSM criteria to diagnose delirium. CAM is the most recognized one, as explained below. Other tools also were developed to assist in delirium diagnosis but also including its severity assessment. For that reason, those tools are included in the following section about "Diagnostic and Assessment of Severity Instruments".

Confusion Assessment Method (CAM)

The Confusion Assessment Method is a diagnostic tool for identification of Delirium that was initially developed by Inouye et al in 1990 based on DSM-III criteria. It has been the most widely used tool to identify delirium and includes a diagnostic algorithm for identification of delirium. Also, it has been the most used tool in delirium research. However, specific training is required to ensure optimum performance. Originally developed by literature review and expert consensus, the CAM was validated considering as the gold standard to the individual patient assessment old age psychiatry experts, based on the DSM-III revised criteria. (10)

The CAM is a diagnostic instrument for identification of delirium. The instrument assesses the presence, severity, and fluctuation of nine delirium features:

- Acute onset;
- Inattention;
- Disorganized thinking;
- Altered level of consciousness;
- Disorientation;
- Memory impairment;
- Perceptual disturbances;
- Psychomotor agitation or retardation;
- Altered sleep-wake cycle.

The CAM diagnostic algorithm is based on the cardinal elements of DSM-III revised criteria for delirium, including four features:

- Feature 1 (acute onset and fluctuation course) and feature 2 (inattention) are essential features;
- Feature 3 (disorganized thinking) or feature 4 (altered level of consciousness) is supported by expert judgment and clinical practice.

The sensitivity of CAM has varied from 46% to 100%, with lower sensitivities reported when CAM was used by nurses or research assistants. CAM is not considered to be a very useful instrument to rate the severity of delirium and consequently is not useful to rate clinical improvement or deterioration.(11)
Because of its accuracy, brevity (5 to 7 minutes), and ease of use by clinical and lay interviewers, the CAM has become the most widely used standardized delirium instrument for clinical and research purposes over the past 16 years.(10)

CAM was not specifically developed for older patients and it has been used in several clinical settings. Different CAM variants have been created considering specificities of different clinical settings, patients' groups and contexts. There are some variants from the original CAM, such as Familiar CAM (FAM-CAM) which was originally developed in 1990, based on the CAM, to provide a method for informant-based assessment of

delirium to determine study eligibility for a largescale prospective cohort.(12) Exists another CAM variant used in intensive care, the CAM-ICU.

Stanford proxy test for delirium (S-PTD)

The S-PTD is a recently presented tool for the recognition of delirium by the Maldonado team from the Standford University and Medical Centre. The tool, still not published, was recently presented in the American Psychiatric Association and European Delirium Association annual meetings in 2016 in Atlanta (USA) and Vilamoura (Portugal) as being quick (<1min) versus 5 minutes with CAM, accurate, comprehensive and simple to administrate. The strong feature of S-PTD is that it eliminates the need of direct patient participation in the assessment. Like 4AT presented below the S-PTD can be applied by the nursing staff; in the end of the shift all the information concerning the nurse-patient interaction during the shift is used to fulfil the scale and diagnose delirium. A previous training period of two weeks was undertaken in the studies performed. S-PTD was effective in identification of delirium, comparing to CAM and psychiatry expert's assessment as gold standard; it was equally effective in identification of both hypoactive and hyperactive delirium which is a great advantage in clinical practice. However, the first S-PTD study was limited to neurological and neurosurgical non elderly patients.

The S-PTD tool was developed combining DSM-5 and ICD-10 (International Classification of Diseases, 10th revision) delirium diagnostic criteria for the first time.
The main advantage of observation based tools, such as S-PTD, is that it can enable the early recognition and diagnosis of delirium in daily clinical practice. Moreover, nurses who participated in the first study reported that S-PTD is easier to apply than CAM. Validation studies on older patients may clarify the utility of this promising tool in older patients.

According to a cut-off score of 4 or more, the S-PTD had a sensitivity of 79%, specificity of 91%, positive predictive value of 70%, and negative predictive value of 94%. Performance of the S-PTD was similar to the CAM in identifying delirium, with a McNemar test P value of .739.

Screening Instruments

4 AT- Assessment test for Delirium and Cognitive impairment

The 4A's Test is a new screening tool for delirium diagnosis specifically designed for older people by MacLullich team in Edinburgh in 2011. (13)It consists of four items: two brief cognitive tests, assessment of level of consciousness, and comparison with basal cognitive status (an acute change in mental state suggests delirium). (14) It was developed to overcome some gaps of previous delirium screening tools which failed to be useful in clinical practice as they required previous training and considerable amount of time per patient. Strong features of 4AT are: brevity (generally <2 minutes), no special training required, simple to administer (including in people with visual or hearing impairment), does not require physical responses, allows for assessment of 'untestable' patients (those who cannot undergo cognitive testing or interview because of severe drowsiness or agitation) and incorporates general cognitive screening to avoid the need for separate tools for delirium and other causes of cognitive impairment.(13)This tool allows assessment of the drowsy patient and delirium superimposed on dementia, frequent conditions in Geriatric wards. A major advantage is that 4AT also allows the assessment of patients with fluctuating level of consciousness, hypoactive delirium and cognitive impairment.

4AT was validated by Bellilli team in hospitalized elderly patients using as gold standard the DSM-IV revised delirium criteria. (13) 4AT was showed to have a sensitivity of 90% and specificity of 84% in screening of delirium in hospitalized elderly patients (Bellilli et al). Therefore, 4AT is a promising tool in delirium screening in geriatric wards that can be used by nursing staff in daily clinical practice. (13)

The reported advantages of the tool were easiness of use, the quickness of the assessment procedure, the absence of previous training requirement, and the ability to assess patients with fluctuating level of consciousness, hypoactive delirium and cognitive impairment.

Key features of 4AT:

- brevity (<2 minutes);
- no special training required;
- allows for assessment of “unstable” patients;
- incorporates brief cognitive teste items.(14)

The 4AT scores 0 to 12. A score of 0 suggests that delirium and/or moderate to severe cognitive impairment is unlikely. Scores between 1 and 3 suggest possible moderate to severe cognitive impairment (that is, corresponding to moderate to severe impairment on dementia screening tools). A score of 4 or above suggests possible delirium.
. It incorporates two items for initial testing for moderate to severe cognitive impairment which means that a separate instrument for this purpose may not be necessary. (13)

Diagnostic and Assessment of Severity Instruments

The delirium rating scale- revised (DRS-R-98)

The DRS-R-98 is a validated tool useful in diagnosis and assessment of delirium. However, it has been mainly presented as a delirium severity assessment tool. Delirium severity is assessed according the presence of a range of symptoms. The DRS-R-98 has been showed to be better for longitudinal studies.(15)
It includes separate items for hypermotor and hypomotor presentations, affect disturbance, language disturbance, long-term memory disturbance, and visuospatial impairment. It has 16-item:13 items concerning the severity of symptoms and 3 items with diagnostic significance. The rating is applicable to the preceding 24 hours.

The severity rating of each item range from 0 (no impairment) to 3 (severe impairment) and a severity score >15 or a total score of >18 is indicative of delirium. In this scale higher scores indicate higher severity of delirium. The severity items can further be classified as cognitive and non-cognitive delirium symptoms.

A strong aspect of the DRS-R-98 is that it differentiates delirium from dementia, schizophrenia, depression, and other medical illness during blind rating, with sensitivity rating from 91% to 100%.(11, 14)

The memorial delirium assessment scale (MDAS)

The MDAS is an instrument to both diagnose delirium and measure its severity according the physician assessment. It has 10 items which assesses disturbances in arousal and level of consciousness, as well as several domains of cognitive functioning (memory, attention, orientation, and disturbances in thinking) and psychomotor activity. This items are rated on a four-point scale (0-3). Information used to complete the MDAS scale can be related to the current interaction between the physician and the patient during the physical assessment or the patient behaviour in the previous hours. Completion of MDAS requires about 10-15 minutes.

The MDAS total scores differs significantly between patients with delirium and those with other cognitive impairment disorders or no cognitive impairment. The diagnosis of delirium is suggested of a score of 13 or more is obtained.(11) MDAS showed 64,1% of sensitivity and 100% of specificity. MDAS has been used in surgical, oncological and palliative care patients.

Other Delirium Assessment Tools

Other useful tools in Delirium assessment

According to the new DSM 5 criteria to diagnose delirium, dementia (or any degree of previous cognitive impairment) and coma must be excluded as being the cause of acute neurological changes.

In order to exclude dementia and coma, other scales that are not specifically used for the screening or diagnosis of delirium can still be useful to clarify the diagnosis. Arousability and premorbid cognitive impairment are features that can be assessed using tools specifically designed for that purpose.

Attention might also be a difficult characteristic to assess and also simple bedside tools have been developed, as described below.

Assessment of Arousability

Altered consciousness has been regarded as a core feature of delirium since the DSM - III. DSM-5 now operationalises 'consciousness' as 'changes in attention'.

However, two dimensions of consciousness have been described in the literature: arousal and attention. Arousal corresponds to level of consciousness. Attention relates to the content of consciousness. Reduced arousal is associated with adverse outcomes. Arousal and attention are hierarchically related: the level of arousal must be sufficient before attention can be reasonably tested. Unarousable patients are unable to be attentive and attention cannot be tested. That is the case of coma and stuporous patients. The 4AT tool takes into account both features arousability and attention.

Arousability is assesses in |1| item- alertness; assessment consists of an attempt to wake up the patient and/or asking for simple information like his name and address.

Attention assessment is the item |3| and consists of ask the patient to tell the months of the year in backward order.

Exploratory findings suggest that **abnormal level of arousal** is a strong indicator of delirium and is strongly associated with inattention as measured by an objective

cognitive test. (6)These findings suggest that acute-onset abnormal level of arousal could be used as a trigger for delirium assessment in routine clinical practice. Arousability assessment tools can precede delirium screening applied in 4ATbut existing tools were just designed for ICU setting, such as Richmond agitation-sedation scale (RASS). RAAS assess the level of sedation and agitation in adult patients admitted in ICU. It scores minimum -5 and maximum +4 points according the patient's responses to verbal and physical stimulation. It can be used by physicians and nurses, taking 15 seconds to perform. **RASS** has a close correlation with the Glasgow Coma Scale. A patient scoring between +4 to -4 is considered to be assessable for delirium.

- **Positive scores**
    - alert and calm (central score)
    - +1-restlessness
    - +2 and +3-agitation
    - +4 combative behaviour

- **Negative scores**
    - -1-Lethargy
    - -2 and -3- poor response to verbal stimulus
    - -4- responsive only to physical stimulus
    - -5-unresponsive

Hyperactive delirium is defined as persisting rating of +1 to +4 during all assessments. Hypoactive delirium is defined as persistent rating of 0 to -3 during all assessments. Mixed subtype delirium is defined as fluctuation between hyperactive and hypoactive RASS values. CAM- ICU administration should be preceded by arousal assessment; if RASS scores between -4 and -5 the CAM-ICU cannot be performed.(11)

Months of the year backwards (MOTYB)

Months of the Year backwards (MOTYB) is a commonly administered bedside cognitive function assessment test which is included in 4AT. It is a rapid (<2minutes) and easy to administer test of cognition that can be applied in the bedside of a patient. It has been

described as a primarily test of attention, as well as a test of concentration, working memory, executive function, cognitive flexibility and central processing speed.

The MOTYB is particularly useful in the diagnose of delirium and associated pathologies in hospitalized patients as it assesses the core feature attention. This is the rationale of its inclusion in 4AT.

The simplicity of the MOTYB has allowed its use in a range of clinical scenarios, including some which require speed and portability of assessment procedures. This tool shows utility as a single and independent measure and as part of composite testing tools, like un 4AT.

Early studies in elderly hospitalised patients with dementia found that the MBTYB was one of seven tests (from a total of 25 tests) that discriminated well between different levels of cognitive impairment.(16)

Assessment / Screening for Premorbid Cognitive Disturbances

Informant questionnaire on cognitive decline in the elderly (IQ CODE)

This retrospective scale has been designed to assess the cognitive level of patients according the information provided by the caregivers. It is a screening questionnaire to assess cognitive decline in elderly and screen for dementia. It can be completed by the relatives or other caregivers of the older persons.

The original version reports to 26 everyday situations in which the person has to use memory and intelligence. Each situation is rated based on the amount of change over the previous 10 or 5 years. Each item is rated on a 5point rating scale, 1 rated as much improved, 2 rated as a bit improved, 3 rated as not much change, 4 indicates a bit worse and 5 indicates much worse functioning. Person with no cognitive decline- average score is 3. Some cognitive decline scores greater than 3.

Studies have shown good correlation between IQCODE and the Mini-Mental State Examination. The IQCODE scores have no relation with a person's level of education or with their premorbid level of intelligence.(11)

Screening tools designed for other health professionals

It is not possible to physicians to screen all the patients for delirium (due to restrictions of time or even expertise. Consequently, many screening instruments have been designed to be used by other healthcare professionals for evaluating the patients for possible delirium. As nurses are the healthcare professionals who spend more time with the patients several screening tools have been specifically designed for them.(11)

NEECHAM confusion scale

This tool is a screening scale that is used by nurses to rate the patient's behaviour while providing routine care to hospitalized patients. This scale has 3 subscales.

Subscale -1 has 3 items and measures cognitive processing (attention, ability to follow command, and orientation) and the rating varies from 0-14 for the subscale;

Subscale-2 has 3 items and measures behaviour (appearance and motor and verbal behaviour) and the rating varies from 0-10.

Subscale-3 has 3 items to rate physiological parameters -stability of vital parameters (temperature, blood pressure, heart rate and respiration), oxygen saturation stability and urinary continence control.

The total score ranges from 0 (minimal responsiveness) to 30 (normal function). A score below 20 points indicates moderate to severe delirium, a score between 20 and 24 suggests mild or early development of delirium. A score of 25 and 26 suggests that the patient is "not delirious", but the patient is at high risk for delirium and a score of 27-30 indicates normal function. The scale takes 10 min to complete. It has good validity, high sensitivity (95%) and specificity (78%). (11)

Nursing delirium screening scale

This screening tool assess disorientation, inappropriate behaviour, inappropriate communication, hallucination, and psychomotor retardation. It is a tool design to be used by a nurse based on clinical observation in routine practice during the hospitalization. Each item is rated on a 3-point scale (0-2) and the total score varies from 0-10. The cut-

off for delirium is 2. It takes 1 min to complete and shows a sensitivity of 85.7% and specificity of 86.8% for the diagnosis of delirium.(11)

Delirium observation screening scale

This tool is based on DSM-IV criteria for delirium and consisted initially of a 25-items scale. It was designed to be used by nurses during the routine patient care in order to identify early symptoms of delirium. The scale was subsequently reduced to 13 items, and is known as DOS-Delirium Observation screening scale. The 13 items are scored dichotomously as “present” or “absent” (total score 0-13). It can be rated each work shift by the nursing staff and the ratings of all the 3 day shifts can be added and the score per day can range from 0-39. The final score is calculated by taking the mean of the 3 shifts and it ranges from 0-13. A score greater than 3 indicates Delirium.(11)

New Technologies applied to the delirium diagnosis

As we know delirium is underdiagnosed mostly because It is under evaluated in hospitalized patients. Innovative approaches can improve delirium diagnosis and are urgently needed.

Delbox

Recently researchers at the LLHW Centre for Cognitive Ageing and Epidemiology (CCACE) and the Edinburgh Delirium Research Group, at the University of Edinburgh, have developed a new, quick and simple method for diagnosing delirium. Together with the company, Eagle Designs, they have designed a computerised testing device, known as 'Delbox', which can be used to help diagnose delirium, by testing inattention, using simple visual tests.

Delbox works by testing inattention, which is the core feature of delirium. The box has two buttons which flash on and off. Patients are asked to either count how many light flashes the device produces over a short period of time or to press a button each time they see one of the buttons light up.

Delbox is the first computerised test specifically designed for detecting inattention, which is the core feature of delirium according new DSM criteria. Its simple and objective scoring system makes it easy for clinicians to use. It also has a robust and portable design, which makes it suitable for bedside testing in a hospital environment, and the retro appearance is intended to appeal to older patients. Delbox was designed to differentiate between delirium and dementia. Assuming that patients with dementia are able to focus their attention for longer periods than patients with delirium. (17)

DelApp

After the creation of Delbox, the Company Eagle Design developed an Android-based software app (DelApp) that recreates Delbox tasks on smartphones. The rationale is that though the Delbox is effective, tests on devices that are universally available potentially have greater impact namely because young doctors are willing to use new technology. Pilot studies performed in general acute wards and ICU units showed that DelApp is effective in assessment of attention, is user-friendly and accepted by patients. (17)

Delbox Image

CONCLUSION

The current overview about delirium screening and diagnosis tools shows that there is still no evidence to consider a single tool the better one to identify delirium in older patients. Most studies do not compare tools and are mainly focused in showing that they are effective in diagnosing delirium according DSM criteria applied by experts on gerontopsychiatry, which still is considered the gold standard in delirium diagnosis. Comparative studies between different tools could be useful to recognise which tools are more effective in specific patient's subsets.

Clinical diagnosis of delirium is the key, namely because there is no single laboratory or imaging test can diagnose delirium. It is wise to consider that the better delirium screening and diagnosis tool will be the one that healthcare professionals are trained to use.

Nevertheless, when comparing the tools, the CAM although it is the most widely used, studied and disseminated and it takes few time to be completed, it seems more difficult to complete by non-psychiatry experts, who may have some difficult to match the patients changes to the features identified in the CAM criteria. For research purposes, it is probably the better option even because it has been used for 16 years, enabling comparisons between centres.

A strong advantage of 4AT is that the instructions given to the healthcare professional to assess each delirium dimension are very clear and easy to understand and perform, which makes 4AT a nurse-friendly tool. Also its layout is very simple. 4AT is therefore a convenient tool to be used in clinical settings where gerontopsychiatry and geriatrics education and skills are low.

The S-PTD has been presented as a promising tool, however it is a 12-item tool and items description might not be easy to translate in patient's symptoms for healthcare professionals who have no specific knowledge about gerontopsychiatry.

Due to the factors mentioned above, 4AT might be a good tool to be established as the standard assessment tools, namely to perform delirium screening by nurses.

Another important conclusion of this review is that clinical entities and diagnostic criteria change over time. Currently is given more importance to the baseline mental status of patients in order to avoid false diagnosis of dementia. DSM 5 delirium criteria is the first version mentioning that the awareness and attention baseline change is a *sine*

qua non condition to diagnose delirium. The new S-PTD already includes an item that specifically addresses this feature (changes from baseline cognition and behaviour); CAM and 4AT do address the acute character of mental functions changes but the baseline change is not assertively mentioned.

To conclude, the authors suggest the 4AT to be implemented in Portuguese medical wards as an easy delirium screening tool.

ATTACHMENTS:

Tables:

Pathophysiological mechanism	Evidence
Neurotransmission	The cholinergic system is very important in cognition and attention, and there is an extensive evidence that support a role for cholinergic deficiency in delirium. Anticholinergic drugs can induce delirium and these drugs are often used in hospitalized patients. Other neurotransmitters are suggested to be involved in the pathophysiology of delirium such as: glutamate, gamma-aminobutyric acid, 5-hydroxytryptamine (5-HT) and norepinephrine are also hypothesized to be linked to delirium.
Inflammation	Clinical evidence suggests that trauma, infection or surgery can lead to increased production of proinflammatory cytokines that can, in susceptible individuals, induce delirium. Those cytokines cause exaggerated responses from microglia causing severe inflammation in the brain.
Acute stress response	High levels of cortisol associated with acute stress have been associated with the onset and maintenance of delirium. Steroids can cause impairment in cognitive function. In elderly patients, feedback regulation of cortisol might be impaired, resulting in higher levels of baseline cortisol and thereby predisposing this population to delirium.
Neuronal Injury	Delirium can be caused by a variety of metabolic or ischemic insults to the brain. Hypoxemia, hypoglycaemia and other metabolic derangements can cause energy deprivation which leads to impaired synthesis and release of neurotransmitters, as well as impaired propagation of nerve impulses across neural networks involved in attention and cognition.
Neuroimaging findings	In elderly patients with delirium attributable to various aetiologies, imaging has revealed marked cortical atrophy in the prefrontal cortex, temporoparietal cortex, and fusiform and lingual gyri in the non dominant hemisphere, and atrophy of deep structures, including thalamus and basal ganglia.

Table 1- Physiopathological mecanismos of Delirium and scientific evidence (1) (2)

Potentially modifiable risk factors	No modifiable risk factors
• Sensory impairment (hearing or vision); • Immobilization (catheters or restraints); • Medications (sedative hypnotics, narcotics, anticholinergic drugs, corticosteroids, polypharmacy); • Acute neurological diseases (acute stroke, intracranial haemorrhage); • Intercurrent illness (infections, iatrogenic complications, severe acute illness, anaemia, dehydration); • Metabolic derangement; • Surgery; • Environment (admission in ICU); • Pain; • Emotional distress; • Sustained sleep deprivation.	• Dementia or cognitive impairment; • Advanced age (>65 years); • History of delirium, stroke, neurological disease; • Multiple comorbidities; • Male sex; • Chronic renal or hepatic disease;

Table 2- Modifiable and nonmodiafiable risk factors for Delirium

DSM-IV Delirium Criteria
A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).
B. The disturbance develops over a short period of time (usually hours to a few days), represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception).
D. The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.
E. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple aetiologies.

Table 3- DSM-5 Delirium criteria

DSM-III (1980)	DSM-IV (1994)	DSM-5 (2015)	Comments
A. Clouding of consciousness (reduced clarity of awareness of the environment, with reduced capacity to shift, focus, and sustain attention to environmental stimuli.	A. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention.	A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)	The cardinal criterion for DSM-5 and DMS-IV includes both inattention and reduced awareness of the environment. Although attention and awareness are important components of normal consciousness, they do not fully represent it.
B. At least two of the following: 1. perceptual disturbance: misinterpretations, illusions, or hallucinations; 2.speech that is at times incoherent; 3. disturbance of sleep-wakefulness cycle, with insomnia or day-time drowsiness; 4 increased or decreased psychomotor activity. C. disorientation and memory impairment (if testable).	B. change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia.	C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception). D. The disturbance in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.	Unlike DSM-IV, DSM-5 criteria specifically excludes coma from being labelled as delirium but suggests that when reduced arousal impairs ability to engage with cognitive testing that this can be considered as severe inattention. DSM-IV and DSM 5 exclude dementia as the primary cause of the disturbance while DSM-5 more broadly includes other neurocognitive disorders besides dementia.
D. Clinical features that develop over a short period of time (usually hours to days and tend to fluctuate over the course of a day.	C..The disturbance develops over a short period of time(usually hours to days) and tends to fluctuate	B.The disturbance develops over a short period of time(usually hours to a few days), represents a change from baselined attention and awareness, and tends to fluctuate in severity during a course of a day.	DSM-5 has a broader list of etiological types.
Evidence, from the history, physical examination, or laboratory tests, of a specific organic factor judged to be etiologically related to the disturbance.	There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.	E. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin, or is due to multiple aetiologies.	Both capture acuity of onset and fluctuation of severity. Change from baseline is noted only in DSM-5 as this relates to attention and awareness. The comparison with baseline cognitive status is a new feature noted in the DSM-5 criteria. The importance of the short period of time in the establishment of delirium and the fluctuation of symptoms is stressed in the new DSM-5 criteria as it changed to the secondo position(D).

Table 4- Comparison between DSM-III, DSM-IV and DSM-5 criteria for Delirium diagnosis.

Delirium screening tool	Criteria on which based	Number of items assessed	Healthcare professionals administrating the tool	Time of administration taken (minutes)	Population tested	Specificity %	Sensitivity %	Assessment Characteristics
CAM	DSM III-R	4/9	Trained clinician	5-7	Elderly, mixed, oncology, palliative and surgical.	63-100%	46-100% (depends on operator experience)	Operator training required to maximize accuracy. Limited assessment of drowsy patient.
DRS-R-98	DSM III	16	Clinician with psychiatry training	20-30	Mixed.	84-92%	91-100% (depends on cut-off score)	Psychiatry specific training required Consensus unclear on cut-off score accepted for positive result Longest time to administer
4AT	DSM IV	4	Anyone	2-3	Mixed.	84,1%	89,7%	Allows assessment of the drowsy patient and delirium superimposed on dementia

Table 5- Overview of the Most Frequently Studied Screening Tools, adapted from Bellelli G, Morandi A, Davis DH, Mazzola P, Turco R, Gentile S, et al. Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people. Age Ageing. 2014;43(4):496-502

DELIRIUM ASSESSMENT TOOLS
Diagnostic Instruments: • DSM • CAM • S-PTD
Screening Instruments: • 4AT
Diagnostic and Severity Assessment Instruments: • DRS-R-98 • MDAS
Other useful tools: • RASS (assessment of arousability) • MOTYB (assessment of cognitive function) • IQCODE (assessment of premorbid cognitive disturbances) • NEECHAM confusion scale (assessment of behaviour by nurses) • Nursing Delirium screening scale (assessment of several cognitive and behavioural symptoms by nurses) • Delirium observational screening scale (assessment of early symptoms of delirium by nurses)
New Technologies: • Delbox • DelApp

Table 6- Delirium assessment tools summarized.

References:

1.Inouye, S., Westendorp, R. and Saczynski, J. (2014). Delirium in elderly people. *The Lancet*, 383(9920), pp.911-922.

2.Kontis V, Bennett JE, Mathers CD, Li G, Foreman K, Ezzati M. Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble. The Lancet. 2017;389(10076):1323-35.

3.Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. Nat Rev Neurol. 2009;5(4):210-20.

4.Sharon K. Inouye, M.D., MPH1, Stephanie Studenski, M.D.2, Mary E. Tinetti, M.D.3, and George A. Kuchel, M.D.4, Geriatric Syndromes: Clinical, Research and Policy Implications of a Core Geriatric ConceptPublished in final edited form as: J Am Geriatric Soc. 2007 May; 55(5): 780–791.

5.Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. The Lancet. 2014;383(9920):911-22.

6.Moraga AV, Rodriguez-Pascual C. Acurate diagnosis of delirium in elderly patients. Curr Opin Psychiatry. 2007;20(3):262-7.

7.Velayudhan L, Ryu SH, Raczek M, Philpot M, Lindesay J, Critchfield M, et al. Review of brief cognitive tests for patients with suspected dementia. Int Psychogeriatr. 2014;26(8):1247-62.

8. Steis, M. and Fick, D. (2011). Delirium Superimposed on Dementia: Accuracy of Nurse Documentation. Journal of Gerontological Nursing, 38(1), pp.32-42.

9.Asthana, S., Halter, J., Hazzard, W., High, K., Ouslander, J., Ritchie, C., Studenski, S. and Supiano, M. (n.d.). Hazzard's Geriatric medicine and gerontology. 1st ed.

10.Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. J Am Geriatr Soc. 2008;56(5):823-30.

11Grover S, Kate N. Assessment scales for delirium: A review. World J Psychiatry. 2012;2(4):58-70.

12.Ely, E., Margolin, R., Francis, J., May, L., Truman, B., Dittus, R., Speroff, T., Gautam, S., Bernard, G. and Inouye, S. (2001). Evaluation of delirium in critically ill patients: Validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Critical Care Medicine, 29(7), pp.1370-1379.

13.Bellelli G, Morandi A, Davis DH, Mazzola P, Turco R, Gentile S, et al. Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people. Age Ageing. 2014;43(4):496-502.
14.De J, Wand AP. Delirium Screening: A Systematic Review of Delirium Screening Tools in Hospitalized Patients. Gerontologist. 2015;55(6):1079-99.
15.Trzepacz, P. (2001). Validation of the Delirium Rating Scale-Revised-98: Comparison with the Delirium Rating Scale and the Cognitive Test for Delirium. Journal of Neuropsychiatry, 13(2), pp.229-242.
16.Meagher J, Leonard M, Donoghue L, O'Regan N, Timmons S, Exton C, et al. Months backward test: A review of its use in clinical studies. World J Psychiatry. 2015;5(3):305-14.
17.Eva Nouzova L-MR, Nikki Duncan, Caoimhe Clarke, Christipher Weir, Jonathan Evans. <LLHW DELBOX case study.pdf>. Geriatric Medicin, University of Edinburg, UK. 2016.

18.Pedro Sá Esteves, Diana Loureiro, Elisabete Albuquerque, Filipe Vieira, Luísa Lagarto, Sandra Neves, Joaquim Cerejeira. Neuropsychiatric symptoms before hospitalization as predictors of delirium onset. 11th Congress of the European Delirium Association.

19. Cristina Braço Forte (1) - Maria João Serpa (1) - Sofia Duque (2) - José Pimenta da Graça (1) Internal Medicine Department, Hospital Beatriz Ângelo, Lisboa, Portugal (1) - Hospital Beatriz Ângelo - Internal Medicine Department, Faculty of Medicine of Lisbon - University Geriatric Unit, Lisboa, Portugal (2) Effectiveness of postgraduate education about Delirium 9th Annual Meeting of the European Delirium Association November 6th - 7th, 2014 Cremona (Italy).